Appl. No. 09/600,125 Amdt. dated July 9, 2003

Reply to Office action of April 10, 2003

This listing of claims will replace all prior versions, and listings, of claims in the application:

## **Listing of Claims:**

Claims 1-51 (Previously cancelled).

52. (Previously added) A method for enhancing the activity of an antineoplastic drug comprising administering an effective amount of a propargylamine to an animal in need thereof, wherein the propargylamine is of the general formula I

$$R_{1} \qquad (CH_{2})_{y}H$$

$$| \qquad /$$

$$R''(CR'_{2})_{x}C \longrightarrow N$$

$$| \qquad \backslash$$

$$R_{2} \qquad (CH_{2})_{z}C = CR_{3}$$

wherein

x is an integer ranging from 0 to 13;

y is an integer ranging from 0 to 5;

z is 1;

 $R_1$ ,  $R_2$  and  $R_3$  are the same or different and represent hydrogen or a straight chain or branched lower alkyl; and

R' and R" are the same or different and represent hydrogen, phenyl or a halogen and pharmaceutically acceptable salts thereof.

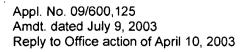
53. (Currently amended) A method according to claim 52 wherein the propargylamine increases for increasing the sensitivity of a tumor to an antineoplastic drug comprising administering an effective amount of a propargylamine to an animal in need thereof, wherein the propargylamine is of the general formula I

$$\begin{array}{c|c}
R_1 & (CH_2)_yH \\
\hline
R''(CR'_2)_xC - N \\
\hline
R_2 & (CH_2)_zC = CR_3
\end{array}$$

## wherein

x is an integer ranging from 0 to 13;

y is an integer ranging from 0 to 5;



z is 1;

R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are the same or different and represent hydrogen or a straight chain or branched lower alkyl; and

R' and R" are the same or different and represent hydrogen, phenyl or a halogen and pharmaceutically acceptable salts thereof.

- 54. (Previously added) A method according to claim 53 wherein the tumor is a drug resistant tumor.
- 55. (Currently amended) A method according to claim 52 wherein the propargylamine protects for protecting normal cells from the cytotoxic effects of the an antineoplastic drug comprising administering an effective amount of a propargylamine to an animal in need thereof, wherein the propargylamine is of the general formula I

## wherein

x is an integer ranging from 0 to 13;

y is an integer ranging from 0 to 5;

z is 1:

R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are the same or different and represent hydrogen or a straight chain or branched lower alkyl; and

R' and R" are the same or different and represent hydrogen, phenyl or a halogen and pharmaceutically acceptable salts thereof

with the proviso that when the propargylamine is R-deprenyl or R-desmethyldeprenyl, the normal cells are not peripheral neurons.

- 56. (Previously added) A method according to claim 52 wherein y is 1.
- 57. (Previously added) A method according to claim 56 wherein the propargylamine is R-2 heptyl-methyl propargylamine (R-2HMP).
- 58. (Previously added) A method according to claim 52 wherein the propargylamine is selected from the group consisting of N-(1-Propyl) N-methylpropargylamine; N-(2-Propyl) N methylpropargylamine; N-(1-Butyl) N-methylpropargylamine; N-(1-Pentyl) N methylpropargylamine; N-(1-Hexyl) N-methylpropargylamine; N-(1-Heptyl) N

methylpropargylamine; N-(1-Octyl) N-methylpropargylamine; N-(1-Nonyl) N methylpropargylamine; N-(1-Decyl) N-methylpropargylamine; N-(1-Undecyl) N methylpropargylamine; N-(1-Dodecyl) N-methylpropargylamine; (R)-N-(2-Butyl) N methylpropargylamine; (R)-N-(2-Pentyl) N-methylpropargylamine; (R)-N-(2-Hexyl) N methylpropargylamine; (R)-N-(2-Octyl) N-methylpropargylamine; (R)-N-(2-Octyl) N methylpropargylamine; (R)-N-(2-Undecyl) N-methylpropargylamine; and (R)-N-(2-Dodecyl) N-methylpropargylamine.

- 59. (Previously added) A method according to claim 52, wherein y is 0.
- 60. (Previously added) A method according to claim 59 wherein the propargylamine is R 2-heptyl-propargylamine (R-2 HPA).
- 61. (Previously added) A method according to claim 59 wherein the propargylamine is selected from the group consisting of N-(1-Propyl) propargylamine; N-(2-Propyl) propargylamine; N-(1-Butyl) propargylamine; N-(1-Pentyl) propargylamine; N-(1-Hexyl) propargylamine; N-(1-Hexyl) propargylamine; N-(1-Decyl) propargylamine; N-(1-Undecyl) propargylamine; N-(1-Dodecyl) propargylamine; (R)-N-(2-Butyl) propargylamine; (R)-N-(2-Pentyl) propargylamine; (R)-N-(2-Hexyl) propargylamine; (R)-N-(2-Hexyl) propargylamine; (R)-N-(2-Decyl) propargylamine; (R)-N-(2-Undecyl) propargylamine; (R)-N-(2-Dodecyl) propargylamine.
- 62. (Previously added) A method according to claim 52 wherein the propargylamine is R-deprenyl.
- 63. (Previously added) A method according to claim 52 wherein the propargylamine is R desmethyldeprenyl.
- 64. (Previously added) A method according to claim 52 wherein the animal is a human.
- 65. (Previously added) A method for enhancing the activity of an antineoplastic drug comprising administering an effective amount of Rasagiline to an animal in need thereof.
- 66. (Previously added) A method according to claim 52 wherein the propargylamine is a chiral compound and is the R-enantiomer.

67. (Currently amended) A method for treating cancer comprising administering an antineoplastic drug and an effective amount of a propargylamine to an animal in need thereof, wherein the propargylamine is of the general formula I

$$R_1 \qquad (CH_2)_yH$$
 
$$| \qquad /$$
 
$$R''(CR'_2)_xC \longrightarrow N$$
 
$$| \qquad \backslash$$
 
$$R_2 \qquad (CH_2)_zC \equiv CR_3$$

wherein

x is an integer ranging from 0 to 13;

y is an integer ranging from 0 to 5;

z is 1:

R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are the same or different and represent hydrogen or a straight chain or branched lower alkyl; and

R' and R" are the same or different and represent hydrogen, phenyl or a halogen and pharmaceutically acceptable salts thereof, with the proviso that the propargylamine is not R-deprenyl, R-desmethyldeprenyl or

Rasagaline.

- 68. (Previously added) A method according to claim 67 wherein the antineoplastic drug is selected from the group consisting of cytosine arabinoside, cis-platinum, cyclophospamide, adriamycin, daunomycin, and 5-fluorouracil.
- 69. (Currently amended) A method according to claim 667 wherein the propargylamine is a chiral compound and is the R-enantiomer.
- 70. (Currently amended) A pharmaceutical composition for treating cancer comprising an antineoplastic drug and an effective amount of a propargylamine of the general formula I:

$$R_1 \quad (CH_2)_yH$$

$$| \quad /$$

$$R''(CR'_2)_xC \longrightarrow N$$

$$| \quad \backslash$$

$$R_2 \quad (CH_2)_zC \equiv CR_3$$

wherein

x is an integer ranging from 0 to 13;

y is an integer ranging from 0 to 5;

z is 1;

R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are the same or different and represent hydrogen or a straight chain or branched lower alkyl; and

R' and R" are the same or different and represent hydrogen, phenyl or a halogen and pharmaceutically acceptable salts thereof, with the proviso that the propargylamine is not R-deprenyl, R-desmethyldeprenyl or Rasagiline.

- 71. (Previously added) A pharmaceutical composition according to claim 70 wherein y is 1.
- 72. (Previously added) A pharmaceutical composition according to claim 71 wherein the propargylamine is R-2-heptyl-methyl propargylamine (R-2HMP).
- 73. (Previously added) A pharmaceutical composition according to claim 71 wherein the propargylamine is selected from the group consisting of N-(1-Propyl) N methylpropargylamine; N-(2-Propyl) N-methylpropargylamine; N-(1-Butyl) N methylpropargylamine; N-(1-Pentyl) N-methylpropargylamine; N-(1-Hexyl) N methylpropargylamine; N-(1-Heptyl) N-methylpropargylamine; N-(1-Octyl) N methylpropargylamine; N-(1-Nonyl) N-methylpropargylamine; N-(1-Dodecyl) N methylpropargylamine; N-(1-Undecyl) N-methylpropargylamine; (R)-N-(2-Pentyl) N methylpropargylamine; (R)-N-(2-Hexyl) N-methylpropargylamine; (R)-N-(2-Heptyl) N methylpropargylamine; (R)-N-(2-Octyl) N-methylpropargylamine; (R)-N-(2-Octyl) N methylpropargylamine; (R)-N-(2-Octyl) N methylpropargylamine; (R)-N-(2-Undecyl) N methylpropargylamine; and (R)-N-(2-Dodecyl) N-methylpropargylamine.
- 74. (Previously added) A pharmaceutical composition according to claim 70, wherein y is 0.
- 75. (Previously added) A pharmaceutical composition according to claim 74 wherein the propargylamine is R-2-heptyl-propargylamine (R-2HPA).
- 76. (Previously added) A pharmaceutical composition according to claim 74 wherein said propargylamine is selected from the group consisting of N-(1-Propyl) propargylamine; N-(2-Propyl) propargylamine; N-(1-Butyl) propargylamine; N-(1-Hexyl) propargylamine; N-(1-Hexyl) propargylamine; N-(1-Hexyl) propargylamine; N-(1-Nonyl) propargylamine; N-(1-Decyl) propargylamine; N-(1-Nonyl)

Undecyl) propargylamine; N-(1-Dodecyl) propargylamine; (R)-N-(2-Butyl) propargylamine; (R)-N-(2-Pentyl) propargylamine; (R)-N-(2-Hexyl) propargylamine; (R)-N-(2-Octyl) propargylamine; (R)-N-(2-Octyl) propargylamine; (R)-N-(2-Decyl) propargylamine; (R)-N-(2-Undecyl) propargylamine; and (R)-N-(2-Dodecyl) propargylamine.

- 77. (Previously added) A pharmaceutical composition according to claim 70 wherein the propargylamine is a chiral compound and is the R-enantiomer.
- 78. (Cancelled) A pharmaceutical composition according claim 70 wherein the propargylamine is R-deprenyl.
- 79. (Cancelled) A pharmaceutical composition according to claim 70 wherein the propargylamine is R-desmethyldeprenyl.
- 80. (Previously added) A pharmaceutical composition for treating cancer comprising an antineoplastic drug and Rasagiline.
- 81. (New) A method according to claim 53, wherein y is 1.
- 82. (New) A method according to claim 55, wherein y is 1.
- 83. (New) A method according to claim 53, wherein the propargyamine is selected from the group consisting of N-(1-Propyl) N-methylpropargylamine; N-(2-Propyl) N methylpropargylamine; N-(1-Butyl) N-methylpropargylamine; N-(1-Pentyl) N methylpropargylamine; N-(1-Hexyl) N-methylpropargylamine; N-(1-Heptyl) N methylpropargylamine; N-(1-Octyl) N-methylpropargylamine; N-(1-Nonyl) N methylpropargylamine; N-(1-Dodecyl) N-methylpropargylamine; (R)-N-(2-Butyl) N methylpropargylamine; (R)-N-(2-Pentyl) N-methylpropargylamine; (R)-N-(2-Hexyl) N methylpropargylamine; (R)-N-(2-Heptyl) N-methylpropargylamine; (R)-N-(2-Octyl) N methylpropargylamine; (R)-N-(2-Decyl) N methylpropargylamine; (R)-N-(2-Undecyl) N-methylpropargylamine; and (R)-N-(2-Dodecyl) N-methylpropargylamine; and (R)-N-(2-Dodecyl) N-methylpropargylamine.
- 84. (New) A method according to claim 53, wherein the propargylamine is selected from R-2-heptyl-methyl propargylamine (R-2-HPA).
- 85. (New) A method according to claim 55, wherein the propargyamine is selected from the group consisting of N-(1-Propyl) N-methylpropargylamine; N-(2-Propyl) N

methylpropargylamine; N-(1-Butyl) N-methylpropargylamine; N-(1-Pentyl) N methylpropargylamine; N-(1-Hexyl) N-methylpropargylamine; N-(1-Heptyl) N methylpropargylamine; N-(1-Octyl) N-methylpropargylamine; N-(1-Nonyl) N methylpropargylamine; N-(1-Decyl) N-methylpropargylamine; N-(1-Undecyl) N methylpropargylamine; N-(1-Dodecyl) N-methylpropargylamine; (R)-N-(2-Butyl) N methylpropargylamine; (R)-N-(2-Pentyl) N-methylpropargylamine; (R)-N-(2-Hexyl) N methylpropargylamine; (R)-N-(2-Octyl) N-methylpropargylamine; (R)-N-(2-Octyl) N methylpropargylamine; (R)-N-(2-Undecyl) N-methylpropargylamine; and (R)-N-(2-Dodecyl) N-methylpropargylamine; and (R)-N-(2-Dodecyl) N-methylpropargylamine.

- 86. (New) A method according to claim 55, wherein the propargylamine is selected from R-2-heptyl-methyl propargylamine (R-2HMP) and R-2-heptyl-propargylamine (R-2-HPA).
- 87. (New) A method according to claim 53, wherein the propargylamine is a chiral compound and is the R-enantiomer.
- 88. (New) A method according to claim 55, wherein the propargylamine is a chiral compound and is the R-enantiomer.
- 89. (New) A method according to claim 53, wherein the animal is human.
- 90. (New) A method according to claim 55, wherein the animal is human.
- 91. (New) A method according to claim 52, wherein the antineoplastic drug is selected from the group consisting of antimetabolites, alkylating agents, antimicrobial antineoplastics, antimicrotubule agents, cisplatinum and its derivatives and the topoisomerase interactive agents.
- 92. (New) A method according to claim 53, wherein the antineoplastic drug is selected from the group consisting of antimetabolites, alkylating agents, antimicrobial antineoplastics, antimicrotubule agents, cisplatinum and its derivatives and the topoisomerase interactive agents.
- 93. (New) A method according to claim 55, wherein the antineoplastic drug is selected from the group consisting of antimetabolites, alkylating agents, antimicrobial antineoplastics, antimicrotubule agents, cisplatinum and its derivatives and the topoisomerase interactive agents.

- 94. (New) A method according to claim 52, wherein the antineoplastic drug is selected from the group consisting of adriamycin, bis (2-chloroethyl)-3-cyclohexyl-1-nitrosurea (BCNU) and 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU), bleomycin sulfate, camptothecin, carmustine, chlorambucil, cisplatinum, cyclophospamide, cytosine arabinoside, daunomycin/daunorubicin, dacarbazine, doxorubicin, 5-fluorouracil, melphalan, mitomycin, mitoxantrone hydrochloride, etoposide, streptozocin and taxol and taxol derivatives.
- 95. (New) A method according to claim 53, wherein the antineoplastic drug is selected from the group consisting of adriamycin, bis (2-chloroethyl)-3-cyclohexyl-1-nitrosurea (BCNU) and 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU), bleomycin sulfate, camptothecin, carmustine, chlorambucil, cisplatinum, cyclophospamide, cytosine arabinoside, daunomycin/daunorubicin, dacarbazine, doxorubicin, 5-fluorouracil, melphalan, mitomycin, mitoxantrone hydrochloride, etoposide, streptozocin and taxol and taxol derivatives.
- 96. (New) A method according to claim 55, wherein the antineoplastic drug is selected from the group consisting of adriamycin, bis (2-chloroethyl)-3-cyclohexyl-1-nitrosurea (BCNU) and 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU), bleomycin sulfate, camptothecin, carmustine, chlorambucil, cisplatinum, cyclophospamide, cytosine arabinoside, daunomycin/daunorubicin, dacarbazine, doxorubicin, 5-fluorouracil, melphalan, mitomycin, mitoxantrone hydrochloride, etoposide, streptozocin and taxol and taxol derivatives.
- 97. (New) A method according to claim 52, wherein the antineoplastic drug is selected from the group consisting of cytosine arabinoside, cis-platinum, cyclophospamide, adriamycin, daunomycin, vinblastine and 5-fluorouracil.
- 98. (New) A method according to claim 53, wherein the antineoplastic drug is selected from the group consisting of cytosine arabinoside, cis-platinum, cyclophospamide, adriamycin, daunomycin, vinblastine and 5-fluorouracil.
- 99. (New) A method according to claim 55, wherein the antineoplastic drug is selected from the group consisting of cytosine arabinoside, cis-platinum, cyclophospamide, adriamycin, daunomycin, vinblastine and 5-fluorouracil.
- 100. (New) A method according to claim 57, wherein the antineoplastic drug is cisplatinum.

- 101. (New) A method according to claim 60, wherein the antineoplastic drug is cisplatinum.
- 102. (New) A method according to claim 84, wherein the antineoplastic drug is cisplatinum.
- 103. (New) A method according to claim 86, wherein the antineoplastic drug is cisplatinum.
- 104. (New) A method according to claim 67, wherein the cancer involves cells mutant in p53.
- 105. (New) A method according to claim 104, wherein the cancer is selected from the group consisting of leukemias, lymphomas (Hodgkins and non-Hodgkins), lung and colorectal carcinomas, melanomas, ovarian cancer, testicular cancer and breast cancer.
- 106. (New) A method according to claim 55, with the further proviso that the propargylamine is not rasagiline.